GSK-3β inhibitor 13

Cat. No.: HY-149054

CAS No.: 2227316-74-5

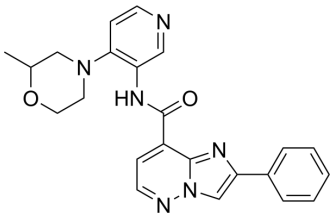
Molecular Formula: $C_{23}H_{22}N_6O_2$

Molecular Weight: 414.46

Target: GSK-3; Tau Protein; AAK1; Pim; PKC

Pathway: PI3K/Akt/mTOR; Stem Cell/Wnt; Neuronal Signaling; JAK/STAT Signaling; Epigenetics; TGF-beta/Smad

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

GSK-3β inhibitor 13 (compound 47) is an orally active and potent GSK-3β inhibitor with blood-brain permeability. GSK-3β inhibitor 13 inhibits GSK-3β and GSK-3α with IC_{50}s of 0.73 nM and 0.35 nM, respectively. GSK-3β inhibitor 13 significantly decreases the phosphorylation of tau (IC_{50}=58 nM), which leads the formation of the neurofibrillary tangles associated with Alzheimer's disease[1].

IC_{50} & Target

GSK-3β 0.73 nM (IC_{50})	GSK-3α 0.35 nM (IC_{50})	PKCθ 0.36 μM (IC_{50})	PIM1 0.38 μM (IC_{50})
AAK1 0.20 μM (IC_{50})			

In Vivo

GSK-3β inhibitor 13 has an exposure of 3.8 μM in plasma and 1.3 μM in brain, resulting in a brain-to-plasma (B/P) ratio of 0.34 [1].

GSK-3β inhibitor 13 (30 mg/kg; p.o.; single dose) results in a 52% reduction in pTau396 in in LaFerla 3xTg-C57BL6 mice[1].

Pharmacokinetic Analysis in Mice[1]

Route	Dose (mg/kg)	CL (mL/mL/kg)	V_{ss} (L/kg)	MRT (h)	$t_{1/2}$ (h)
i.v.	2	3.8	1.1	4.8	5.2

Route	Dose (mg/kg)	AUC_{tot} (μM·h)	C_{max} (μM)	F (%)
p.o.	10	68.3	7.8	64

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Hartz RA, et al. Design, Structure-Activity Relationships, and In Vivo Evaluation of Potent and Brain-Penetrant Imidazo[1,2-b]pyridazines as Glycogen Synthase Kinase-3 β (GSK-3β) Inhibitors. J Med Chem. 2023 Mar 23;66(6):4231-4252.

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